Paul-Louis Simond and his discovery of plague transmission by rat fleas: a centenary

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Since the large epidemics during the 19th and early 20th centuries, plague has never disappeared and the World Health Organization continues to report its sporadic occurrence across both Eastern and Western continents. In 1994 India was struck by an epidemic that caused great disruption.

Four years after Yersin identified the plague bacillus *Yersinia pestis*[1], Paul-Louis Simond discovered that the rat flea was the vector for the disease. When Simond, like Yersin a member of the Pasteur Institute (*Pastorien*), reported his finding in 1898 it raised passionate controversy, especially in the English and French medical communities, and his contribution was never fully acknowledged.

EARLY WORK

Paul-Louis Simond (Figure 1) was born in Beaufort sur Gervanne (Drôme Department, France) in 1858. After medical studies in Bordeaux, he joined the Naval Medical Corps (Médecin de Première Classe des Colonies) and was posted to French Guyana and the Far East. He was 37 in 1895 when he arrived at the Pasteur Institute in Paris where he followed Émile Roux's teaching and worked in Élie Metchnikoff's laboratory. During this time Simond studied coccidians in the intestinal flora of various animals and noticed that structures called 'flagella' made these parasites motile like spermatozoa[2]. He hypothesized that 'the flagellum was characteristic of a male sexual element that functions to fertilize the female element'[3]. An English colleague Ronald Ross, who was at that time studying malaria in India, denied that Simond's flagellum-gamete concept had any scientific value[4].

In March 1897, at Émile Roux's request, Simond travelled to India (Bombay and Cutch-Mandvi in 1897; Jurrachee in 1898 [subsequently Karachi in Pakistan]) to replace Yersin in fieldwork. At this time Asia was experiencing a large plague pandemic and Simond's task, which he accepted with enthusiasm, was to help test the new Pasteur antiserum prepared from live cultures of *Y. pestis* (Figure 2). After the initial encouraging results with serotherapy, subsequent tests were unsuccessful. Nevertheless, Simond was undaunted in his efforts to continue the work begun by Yersin. He walked day and night in the gloomiest areas of Bombay to find infected patients with the help of the French Consul, Pilinski, who knew the city particularly well[5].

During his assignment in India, Simond came to doubt the validity of the various modes of plague transmission so far described. His English, Russian, German and Italian colleagues thought that infection was spread via the excreta of human beings as well as rodents and that the plague bacillus was transmitted by contaminated dust absorbed through inhalation, ingestion or skin wounds. Instead

Figure 1 **Paul-Louis Simond (Archives of Pasteur Institute)**

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Simond had noted that a large proportion of patients presented at an early stage of the disease with a skin phlyctena—a small blister containing fluid and plague bacilli. Simond hypothesized that this small phlyctena was the invasive site that subsequently got larger to become the necrotic buboe (*le charbon pesteux*). He called the small primary lesion 'precocious phlyctena' (*phlyctène précoce*) and wondered whether it could be related to an insect bite, the insect then being the vector for the disease. At the time, this concept for plague transmission was entirely new and was received with scepticism. There was some support, however, from Simond's mentor Charles-Louis Alphonse Laveran—the first man to observe malaria parasites in blood (Ross and Grassi established later the role of mosquitoes in the transmission of malaria). Simond thought that the cockroach could be the vector but he rapidly excluded it as insufficiently mobile and instead focused his attention on the rat flea. It required courage or even temerity to manipulate dead rats with bare hands and pick up their fleas in soaped water[6], but Simond was rewarded. He observed that the fleas when examined under a microscope were full of bacilli. At the same time, a Japanese scientist, Ogata[7], made the same observation but failed to relate this finding to plague transmission. Simond acknowledged Ogata's work in 1905[8].

THE EXPERIMENT IN KARACHI

In 1897, Simond went to Saigon and there he prepared an experimental protocol that he conducted next year in Karachi in the Hotel Reynolds where he found some space to work[9]. Simond described his experiment (in the English translation by Crawford[4]) as follows:

Without delay I proceeded to the experiment I had in mind since the time in Cutch-Mandvi when I had discovered Yersin's bacillus in the digestive tract of fleas taken from plague-ridden rats. I prepared a device consisting of a large glass bottle whose bottom was covered with sand, which would absorb the urine of the rats. The lid consisted of wire mesh covered with fabric held tightly to the neck of the bottle with a drawstring. I was fortunate enough to catch a plague infected rat in the home of a plague victim. In the rat's fur there were several fleas running around. I took advantage of the generosity of a cat I found stalking the hotel premises, borrowing some fleas from it. Once the sick rat was in the bottle, I deposited upon it the cat's fleas from a test tube. I was thus quite sure the rat would be covered with parasites.

After 24 hours the animal I was experimenting on rolled up into a little ball, with its hair standing on end; it seemed to be in agony. I then introduced into the bottle a small metal cage containing a perfectly healthy young Alexandria rat caught several weeks before and kept sequestered from any danger of infection. The cage was suspended with the inside of the bottle several centimeters above the layer of sand. The cage had three solid sides, but the other three sides were covered by wire screen with a mesh size of about six millimeters. The rat inside the cage could not have any contact with the sick rat, the wall of the bottle or the sand.

The next morning the sick rat had died without having moved from where it had been the day before. I left its body in the bottle for one more day. Then I carefully removed it, plunged it into alcohol and performed an autopsy. The blood and organs all contained an abundance of Yersin's Bacillus. During the next four days the other Alexandria rat remained imprisoned in its cage and continued to eat normally. About the fifth day, it seemed to have difficulty moving. By the evening of the sixth day it was dead. An autopsy of this one (previously uninfected rat) revealed buboes both inguinal and axillary. The kidney and liver were swollen and congested. There were abundant plague bacilli in the organs and blood. That day, 2 June 1898, I felt an emotion that was inexpressible in the face of the thought that I had uncovered a secret that had tortured man since the appearance of plague in the world.

The mechanism of the propagation of plague includes the transporting of the microbe by rat and man, its transmission from rat to rat, from human to human, from rat to human and from human to rat by parasites. Prophylactic measures, therefore, ought to be directed against each of these three factors: rats, humans and parasites. I subsequently repeated the same experiment with similar results.

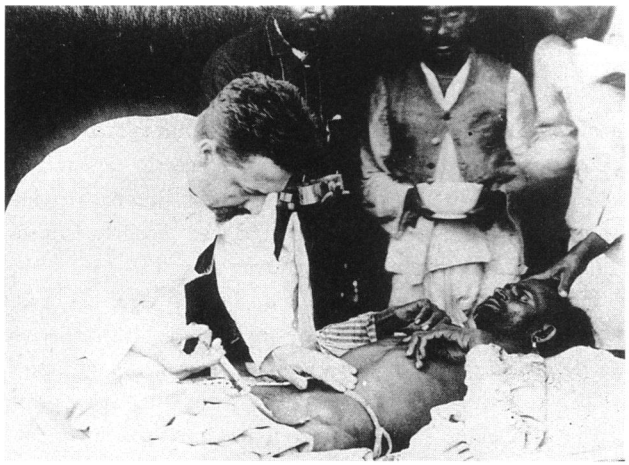

Figure 2 **Simond injecting the Pasteur anti-plague serum on 6 June 1898 in Karachi (Marc Simond's private collection)**

SCEPTICAL RESPONSES

Simond's publication of his results was received with scepticism even by some of his closest colleagues. C Mathis[10], who was enrolled in the French Naval Army, reported one of the senior doctors saying: 'What is this story of fleas told by magician Simond? Do you believe in it?' (This was a reference to the gospels, *Acts* VIII 9–24, where Simon the magician attempted to buy the Holy Spirit from the disciple Peter. The term simonie comes from this story and means the smuggling of holy things). Quite possibly much of the scepticism was related to Franco–English rivalry, as suggested by Crawford[4]. Simond was often at loggerheads with the English authorities; in Karachi the English refused to let him enter the hospitals and he complained bitterly about this in a letter addressed to Émile

Roux, dated 31 August, 1898. By contrast, Simond received a warm welcome from English colleagues in Bombay and Cutch-Mandvi, and in an article published in 1936[9] he paid tribute to their help.

One reason for the scepticism about Simond's claim was the difficulty of reproducing the experiment; contemporary scientists such as J A Thomsom[11] in Sydney and Verjbitsky[12] in Kronstadt tried and failed. It was only in 1903 that Simond's conclusions were fully confirmed by Gauthier and Raybaud in Marseilles[13], who provided evidence that the disease could not be transmitted in the absence of fleas (Figure 3). Another factor in the reluctance to accept Simond's theory stemmed from the association between plague and the poor. Since the poor tended to live in remote areas where hygiene standards were low the traditional theories of direct transmission through absorption were difficult to refute. The doctors most resistant to Simond's ideas were Europeans; the local epidemiologists (*les épidémiologistes debouts*—the standing epidemiologists, as Mollaret[14] described them) were more sympathetic.

At the time of Simond's pioneering work in the late 19th century the medical community was not ready to accept that any biting insect could act as a vector for disease; instead most clinicians believed that 'miasmas' formed the main transmission path for infectious diseases. Further, with specific regard to the role of rat fleas, they understood from naturalists that these parasites did not bite human beings. There were some pioneers, however, who did accept that the transmission cycle for some infectious diseases could involve other living creatures. Finlay in 1864, and before him Beauperthuy, had hypothesized that the amaril virus could be conveyed to humans by mosquitoes, and this was demonstrated at the beginning of the present century by the American Mission in Cuba and by the Pasteur Institute in Brazil (which was directed by P L Simond). In 1878, Manson established the role of mosquitoes in the transmission of filariasis. In 1884, Bruce recognized the role of glossina in the transmission of animal trypanosomiasis. Ronald Ross conducted his work on the malarial parasite during the same period as Simond, with whom he exchanged letters.

It was in the early part of the 20th century that Tiraboschi[15] pointed out that Simond's experiment failed to explain the mode of entry of the plague bacillus into the host subcutaneous tissue. The mechanisms were elucidated in 1914 by two British scientists, A W Bacot and C J Martin at the Lister Institute[16]. Their work demonstrated that fleas (*Xenopsylla cheopis*) get infected when ingesting the blood of a diseased rat or human being. Yersin's bacilli then proliferate rapidly in the flea's foregut, also called the proventriculus, where they form an obstructive mass. At subsequent bites the ingested blood is unable to pass beyond the obstruction and is regurgitated together with Yersin's bacilli into the host's skin. Simond in his original publication in 1898 did not deny the inadequacies of his work and reported:

> While I admit that this theory [transmission by flea] has not yet the full weight of demonstrated fact, we believe that the diverse forms of spontaneous plague, in humans and animals, comes normally from a single mode of infection: intracutaneous parasitic inoculation. Nevertheless, new research is needed before we attribute the exclusive role to it. Nor do we know anything about the changes undergone by the microbe in the body of the parasite. Is the virulence increased, preserved or lessened? Is preservation (of virulence) long or short?
>
> One can suspect that the natural history of fleas, their greater or lesser number according to local conditions, ought to play a major role in the development and in the gravity of the epidemic, and perhaps furnish the solution to the problem of recrudescence of the disease, as yet incompletely resolved.[4]

It was suggested in 1942 by Lowe[17] that most of Simond's ideas and conclusions were plagiarized by others from his publication in 1898. Captain W G Liston, of the British (Indian) Commission, published in the *Indian Medical Gazette* (1906) a report on the epidemiology and transmission of plague in which many of the conclusions were remarkably similar to those enunciated in Simond's 1898 publication[4] with almost no reference to Simond's work. Hankin (1905)[18], a member of the English group working in India in 1898, did acknowledge Simond's findings but expressed some doubts about their scientific merit, as did Heiser[19], an American doctor some 30 years later. It was only after the monumental work done by the English Commission[20] in India, in 1906 and during the following years, that the mechanisms of plague transmission were finally accepted by the scientific world.

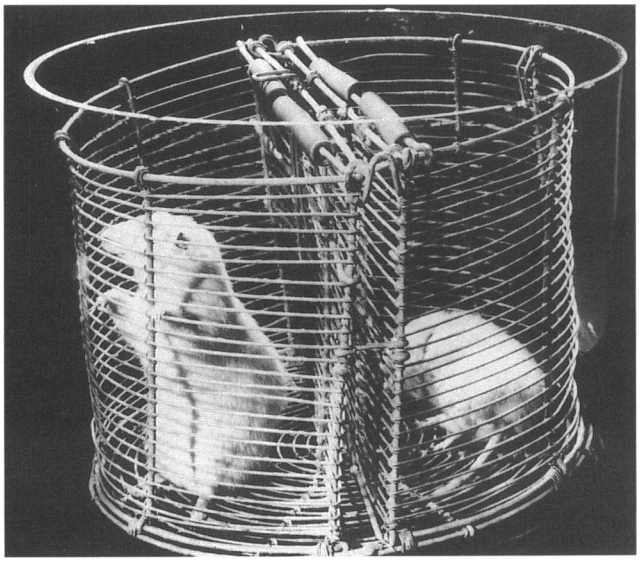

Figure 3 **Experimental material of Gauthier and Raybaud[13] (HH Mollaret's private collection)**

WITHOUT HONOUR IN HIS TIME

Why did Simond's discovery encounter such scepticism? One probable reason is that his contemporaries did not fully understand his methodology. This apart, the number of tests was small, there was the unfortunate difficulty others had in reproducing the work, and the experiment had the critical flaw of being insufficiently controlled. Although Simond reported that, in the absence of fleas, a contaminated rat could not transmit the disease to a normal rat, the evidence was found unconvincing by the medical community. It was thus unsurprising that general acceptance of plague transmission by fleas had to await Gauthier and Raybaud's[14] validation of Simond's work. That Simond provided incomplete evidence to a small, incestuous and jealous community at a time when there was more confidence in 'miasmas' than in vectors of disease may well explain why his contribution was so poorly received.

Simond was an intuitive thinker who contributed a vision, beyond his time, that correctly connected fleas with plague. More than that he displayed courageous dedication in independently providing experimental support for what was at the time a radical concept. His work was the foundation for present-day understanding of how plague is transmitted. Simond abandoned research into plague quite soon after publishing his experimental work and abandoned all scientific activities 15 years later. A hundred years after his original work, when knowledge about plague infection is still woefully incomplete, we should pay tribute to his contribution in understanding a disease that continues to cause suffering and death around the world.

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